

Genetic dissection of human cellular reprogramming to pluripotency

Grant Award Details

Genetic dissection of human cellular reprogramming to pluripotency

Grant Type: Basic Biology IV

Grant Number: RB4-06028

Project Objective: To understand the molecular and cellular mechanisms that underlie the process of human iPS cell generation, particularly with respect to the naive state

Investigator:

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Institution:	University of California, San Francisco
Type:	PI

Award Value: \$1,184,883

Status: Closed

Progress Reports

Reporting Period: Year 1

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Reporting Period: Year 3

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Grant Application Details

Application Title: Genetic dissection of human cellular reprogramming to pluripotency

Public Abstract:

It is now possible to turn adult differentiated cells from a patient into human induced Pluripotent Stem (iPS) cells. These iPS cells hold enormous promise for new therapies in Regenerative Medicine, because they can be coaxed in the laboratory to become any cell type in the human body. While this is a spectacular property, we understand very little about the basic biology of generation of human iPS cells. This is a major gap in our understanding of arguably the most promising new avenue in Regenerative Medicine today. An understanding of the molecular and cellular processes that govern iPS cell generation will be essential for the development of safe and efficient therapies using iPS cells in the clinic.

Research in biological model organisms like fruit flies or mice has shown that unbiased genetic screens, where the entire genome is assessed to discover genes that regulate particular processes, are an enormously powerful tool in basic biology studies. Gene silencing using RNA interference (RNAi) opens the opportunity to perform genetic screens in human cells. Our lab has recently carried out an unbiased genome-wide RNAi screen in the process of turning human skin cells into iPS cells. This extensive screen has already revealed several novel genetic regulators of human iPS cell generation, some of which have been preliminarily studied further. We propose to follow-up on this RNAi screen to gain a comprehensive understanding of the basic biology of human iPS cell generation.

Statement of Benefit to California:

Pluripotent stem cells may provide new treatments for devastating and presently incurable conditions such as diabetes, Parkinson's disease, muscular dystrophies, spinal cord injuries, and many other diseases. The ability to generate induced Pluripotent Stem (iPS) cells from differentiated cells of an adult patient provides a major new tool to study degenerative diseases in the lab, discover new drugs, or develop cells for transplantation. However, we lack an understanding of the basic biological mechanisms that underlie the generation of iPS cells. Our proposal aims to use an unbiased approach to understand the genes that regulate the generation of human iPS cells.

The development of human pluripotent stem cell-based therapies will significantly increase the options available in the California health care system. These new therapies are expected to reduce the long-term health care costs to California by providing cures to degenerative diseases that are currently chronic and require expensive periodic treatment.

Our research is also expected to stimulate the development of biotechnology industry focused on clinical applications of iPS cell technology. Such development will be of great benefit to California by attracting high-skill jobs and tax revenues, and by making the State a leader in a field that is poised to be the economic engine of the future. The State of California will also stand to benefit from the intellectual property generated by this research.

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